55 | Cerebrovascular Disease

DAVID C. GOOD

Definition

A neurologic symptom or symptom complex caused by cerebral ischemia or hemorrhage is commonly called a *cerebrovascular accident* (CVA), or stroke. The cardinal clinical features are sudden or subacute onset and (except for subarachnoid hemorrhage) focal neurologic deficit. Depending on when the patient is seen and the underlying cause, the deficit may be *stable, progressive,* or *completely resolved.* Except for these common features, cerebrovascular diseases are a very diverse group of disorders that are further classified according to etiology, location, and duration of symptoms.

Cerebrovascular diseases are subdivided into ischemic events and *cerebral hemorrhages,* with many etiologies for each (Table 55.1). Ischemic events are further classified according to whether symptoms occurred in the *carotid* or *vertebrobasilar* distribution (Table 55.2) and by the duration of symptoms. *Transient ischemic attacks* (TIAs) seldom last more than a few minutes and never more than 24 hours. In *ischemic stroke,* the neurologic deficit has been present more than 24 hours and may be progressive, stable, or resolving.

Technique

A history of cerebrovascular disease is important because specific therapy may be indicated to prevent further events, and because the history of cerebrovascular disease may be a "marker" for other underlying disease, especially coronary artery disease.

A cerebrovascular event usually results in a patient's seeking medical attention. Patients with TIAs may not seek help, however, and a history of TIAs may come to light only by asking, "Have you ever had any temporary episodes of weakness, numbness, visual problems, or speech difficulty?" Because the ophthalmic artery is a branch of the carotid, the syndrome of amaurosis fugax (fleeting blindness) is a risk factor for other carotid events. Therefore, patients should be asked if they have ever temporarily lost vision in one eye or had a sensation that a shade was being pulled down over the vision of one eye. A past history of a completed stroke can usually be elicited by merely asking, "Have you ever had a stroke?" a term understood by a large percentage of the population. Occasionally, more detailed questioning about specific persistent neurologic symptoms is necessary.

The patient should be encouraged to relate the story of the event spontaneously in his or her own words. More direct questioning may be necessary to assess symptoms at onset, whether or not they progressed, and how long they lasted. Ask if medical help was sought, diagnostic procedures were performed, or any conclusive diagnosis was made. Questions aimed at differentiating between ischemic stroke and hemorrhage should be asked: "Was there headache, stiff neck, vomiting, or clouding of consciousness at onset?" For ischemic events, the vascular system affected should be determined by asking about specific symptoms caused by dysfunction of the carotid or vertebrobasilar systems. The time since the last event is important because the risk of ischemic stroke is greatest in the weeks immediately following TIAs.

The most common cause of ischemic stroke is atherosclerotic disease. Hence, the patient should be questioned about risk factors, especially hypertension. Other causes of ischemic stroke should always be kept in mind (especially

Table 55.1
Etiologies of Stroke

Ischemic
Extracranial atherosclerosis
Intracranial atherosclerosis
Embolism from heart
Intracranial vasculitis (several types)
Increased blood viscosity or coagulability
Complicated migraine
Hypertensive arteriolar disease (lacunar stroke)
Fibromuscular dysplasia
Carotid dissection
Hemorrhage
Hypertension (primary hypertensive hematoma)
Saccular aneurysm
Arteriovenous malformation
Anticoagulant therapy
Bleeding dyscrasias
Amyloid angiopathy
Hemorrhage into brain tumor
Mycotic aneurysm
Idiopathic

Table 55.2
Symptoms of Ischemic Stroke

Carotid distribution
Hemiparesis or monoparesis
Facial weakness
Hemisensory numbness or neglect
Aphasia
Dysarthria
Amaurosis fugax (fleeting blindness of one eye)
Vertebrobasilar distribution
Vertigo
Dysarthria
Dysphagia
Diplopia
Homonymous hemianopsia
Total blindness (cortical blindness)
Alternating or bilateral weakness
Alternating or bilateral numbness
"Crossed" weakness or numbness (ipsilateral face and contralateral body)
Gait ataxia
Limb dysmetria

emboli from a cardiac source), since treatment is different. Therefore, a history of chest pain, symptoms suggestive of MI, congestive cardiomyopathy, valvular disease, or atrial fibrillation should be sought. If symptoms have occurred in multiple vascular distributions, embolic events related to cardiac disease should especially be considered. Any history of recent illness or trauma should be sought in case the patient might have one of the other rare causes of ischemic stroke.

Recognizing the special situation of subarachnoid hemorrhage is critical because recurrent hemorrhage is fatal in a high proportion of cases. There are often no focal neurologic signs, only a sudden severe generalized headache, often followed by a stiff neck, vomiting, and altered consciousness.

Finally, ask if there is residual deficit from any previous event; the patient's current functional capacity should be assessed to assist in planning rehabilitative efforts.

Basic Science

Cerebrovascular diseases are a heterogeneous group of disorders with a variable natural history. Outcome depends on many factors, including the underlying pathophysiology, collateral cerebral circulation, and concurrent illness, especially heart disease.

About 80% of all cerebrovascular events are ischemic in origin, and most are associated with atherosclerotic disease. The risk of an ischemic event increases with age and is correlated with both systolic and diastolic blood pressure, diabetes, and a history of ischemic heart disease or previous stroke. All epidemiologic studies have identified hypertension as the most important risk factor for stroke. Correlation with cigarette smoking and hyperlipoproteinemia is less conclusive. Although stroke is still the third leading cause of death in the United States, the incidence is declining, a fact that has been attributed to better identification and control of hypertension.

Atherosclerosis commonly involves the large extracranial vessels that arise from the aortic arch. Although the carotid bifurcations are most frequently involved, atherosclerosis can also occur at the origins of the common carotid or vertebral arteries or in the intracranial vessels, including the carotid siphon and the basilar artery. Atherosclerosis probably results in ischemic symptoms through several mechanisms. The most widely accepted is platelet activation and aggregation at the site of an ulcerated complex atherosclerotic plaque, with production of thromboxane A_2 from arachnidonic acid resulting in further platelet aggregation. Aggregated platelets can embolize, with specific symptoms dependent on the vessel of embolization. The severity of symptoms depends on the duration of vessel occlusion and the degree of collateral flow through tiny leptomeningeal and other end artery anastomoses. Atherosclerosis may also result in vessel stenosis or occlusion. In this situation, symptoms depend largely on how rapidly stenosis develops and the extent of collateral flow available through the circle of Willis and from extracranial–intracranial anastomoses. The availability of collaterals varies considerably among different people; thus, the same degree of stenosis or occlusion can result in very different symptoms. For example, total occlusion of the internal carotid artery may be asymptomatic in one individual, but result in a disastrous stroke in a patient with congenital absence of portions of the circle of Willis. Other factors that are probably important in determining outcome are blood viscosity, blood glucose, blood oxygen carrying ability, and tissue metabolic demand.

Often, ulcerated plaque and stenosis coexist. Most symptoms probably result from embolization since vessel stenosis must be 75% or greater to account for symptoms on a hemodynamic basis. In some patients, a different mechanism may result in symptoms. Pathologic examination of surgical specimens of atherosclerotic plaque removed during carotid endarterectomy shows a high frequency of recent hemorrhage into the plaque, an event that may have precipitated acute stenosis or embolization.

Stenosis of small intracranial arteries can also result in ischemic symptoms. Patients with hypertension or diabetes can develop atherosclerosis of small intracranial arteries. A more common occurrence is the development of hypertension-related lipohyalinosis and fibrinoid necrosis in small end arteries and arterioles. When this results in occlusion, there is no available collateral flow, and a tiny "lacunar stroke" results. Among the many lacunar syndromes are pure motor hemiparesis with or without dysarthria (due to lesions of the internal capsule or pons) and pure sensory stroke (due to lesions in the thalamus). Patients with lacunar strokes almost never have field defects, aphasia, or other higher cortical function loss.

Emboli from the heart cause 10 to 20% of ischemic strokes. Although many cardiac conditions predispose to cerebral embolization (Table 55.3), the two most common are atrial fibrillation and acute myocardial infarction. The risk of stroke is increased five times in patients with atrial fibrillation and fifteen times if there is associated mitral stenosis. Strokes complicate acute myocardial infarctions approximately 2% of the time. The risk is highest in patients with large infarctions, those with congestive heart failure, or those with anterior infarctions where there is hypokinesis of the left ventricular apex. Emboli usually lodge in end arteries that have poor collateral circulation and therefore often cause major neurologic deficits. The middle cerebral artery distribution is usually affected.

Other rare causes of ischemic stroke include hematologic disorders (polycythemia, thrombocytosis, dysproteinemias, sickle cell disease), fibromuscular dysplasia, carotid dissections, and intracranial vasculitis of several etiologies (lupus erythematosus, giant cell arteritis, syphilitic arteritis, gran-

Table 55.3
Cardiac Conditions Associated with Embolization

Atrial arrhythmias
Atrial fibrillation
Sick sinus syndrome
Valvular heart disease
Valvular vegetations
Rheumatic valvular disease
Prolapsed mitral valve
Mitral annulus calcification
Prosthetic heart valves
Cardiac tumors
Myxoma
Ventricular endocardial thrombi
Acute myocardial infarction
Severe cardiomyopathy
Ventricular aneurysm

ulomatous angiitis). Clinical clues and past history will usually help identify these unusual conditions.

Ischemic events are divided into brief, completely reversible events called transient ischemic attacks (TIAs) and completed strokes. While the therapeutic goals of the latter are aimed at preventing and treating complications and maximizing recovery through rehabilitation, the therapeutic goal for TIAs is prevention of more serious events. TIAs are usually caused by small platelet or cholesterol emboli that temporarily occlude a vessel, then "break up" and move distally. This process may actually be visualized ophthalmoscopically in the branches of the ophthalmic artery following amaurosis fugax. TIAs are known risk factors for subsequent ischemic stroke, with 10 to 40% of patients developing stroke. Unfortunately, there is no uniformly reliable way to predict which patients will go on to infarction. The risk is highest the first 2 months after a TIA, and rapid therapeutic intervention is indicated. Risk of stroke is especially high in cases of "crescendo TIAs," which sometimes precede total vessel occlusion.

The development of saccular aneurysms of the circle of Willis is thought to occur gradually at bifurcation sites where the arterial media may be congenitally absent. The internal elastic lamina at these locations becomes fragmented, possibly accelerated by atherosclerosis. Aneurysms have a predilection for certain locations, especially the posterior communicating artery, anterior communicating artery, and middle cerebral artery. They are multiple in 20% of cases. Progressive enlargement seldom causes symptoms unless the aneurysm compresses an adjacent structure, for example the oculomotor nerve by a posterior communicating artery aneurysm. Aneurysms may be found incidentally at autopsy, and asymptomatic aneurysms discovered in patients being evaluated for other conditions rupture at a rate of 2 to 4% per year. In patients who have already suffered a subarachnoid hemorrhage, the risk of rebleeding is high during the first 7 to 10 days, then drops off slowly to 2 to 4% per year after the first 6 months. Rebleeding should be prevented at all costs, since the mortality rate is as high as 50%.

Congenital cerebral arteriovenous malformations (AVMs) consist of malformed, thin-walled, hyalinized vessels with adjacent gliosis and neuronal degeneration. AVMs may never rupture and often come to clinical attention as a cause for a seizure disorder rather than because of hemorrhage. The mortality and rebleeding risk are less than for saccular aneurysms. The peak incidence of hemorrhage from AVMs is under age 30, while the incidence of aneurysm rupture peaks between ages 40 and 60.

The etiology of intracranial hematomas due to hypertension is unknown. In many cases, lipohyalinosis and fibrinoid necrosis probably cause weakness of the arteriolar media with subsequent rupture. Some events may be due to microscopic Charot–Bouchard aneurysms of small arteries and arterioles. Most hypertensive hematomas do not recur. A syndrome of recurrent intracerebral hemorrhage has been described in the syndrome of amyloid angiopathy, a condition of unknown etiology consisting of amyloid deposits in vessel walls in elderly persons and often associated with dementia. Intracerebral hemorrhage also occurs with trauma, anticoagulant use, and bleeding dyscrasias. Rare causes include hemorrhage into a brain tumor or infarction. In some patients, the cause of hemorrhage cannot be determined. Although many intracerebral hematomas are devastating events, patients with small hematomas have a reasonable prognosis for a functional recovery.

Clinical Significance

Because cerebrovascular disorders are a diverse group of illnesses that are managed in very different ways, an accurate diagnosis is critical. The following points are important for proper diagnosis and management:

1. Establish that a cerebrovascular event actually occurred, and determine the location of the event.
2. Decide if the event was ischemic or hemorrhagic.
3. Determine what steps are necessary for medical stabilization of the patient.
4. Determine the underlying pathophysiology that caused the event (e.g., atherosclerosis, embolus, aneurysm).
5. Determine what can be done to prevent future, possibly more devastating, events.
6. Decide if the occurrence of the cerebrovascular event may indicate an underlying disease (especially cardiac diseases).
7. When a fixed deficit already exists, establish the patient's potential for rehabilitation.

Occasionally, other conditions can mimic cerebrovascular events. Primary or metastatic *tumors* usually progress insidiously, but occasionally symptoms begin acutely because of rapid tumor growth, hemorrhage into a tumor, or a seizure followed by focal neurologic signs. *Seizures* may be especially confusing because they may be the first symptom of a brain tumor, but also accompany acute stroke in 5% of cases. Although neuroradiologic procedures usually differentiate between stroke and tumor, occasionally small tumors are overlooked, and a follow-up CT or MRI scan is suggested in ambiguous cases. Distinguishing between TIA or stroke and *migrainous phenomena* may also be difficult. The latter usually occur in younger individuals, with a clear history of vascular headaches. They have a more insidious onset than TIA or stroke, and a gradual "spread" of symptoms. While migrainous events are usually transient, permanent neurologic deficits, such as hemiparesis, sensory deficit, and aphasia, are occasionally attributed to migraine. Diagnostic problems may arise when transient visual or neurologic events accompanied by headache occur in older patients. Although an attempt should be made to decide if an episode was migrainous by inquiring about rate of progression of a neurologic symptom, previous history of vascular headaches, history of "classic" visual events such as scintillating scotoma, and family history of migraine, in some cases no clear differentiation can be made. A final difficult area are patients with vague or *nonlocalized neurologic events*. The definition of a CVA as the acute or subacute onset of a focal neurologic event should be remembered, and patients with syncope, transient confusion, anxiety, and nonspecific symptoms should not be given this diagnosis.

In patients with ischemic stroke or TIA, the underlying cause often determines therapy. Therefore, it is necessary to distinguish between events due to atherosclerosis, embolic events of cardiac origin, lacunar strokes, and strokes due to rare conditions.

Atherosclerosis is a systemic arterial problem of which stroke and TIA are manifestations. The presence of known risk factors raises the possibility that such an event has an atherosclerotic etiology. About 10 to 20% of atherosclerotic strokes are preceded by TIAs. The presence of a carotid bruit is associated with an increased risk of atherosclerotic stroke, although not necessarily in the distribution of the vessel over which the bruit is heard.

The diagnosis of *embolic stroke* is best made in the presence of one of the cardiac conditions associated with systemic embolization. All patients with ischemic TIA or stroke should be questioned and examined for evidence of atrial arrhythmias, recent myocardial infarction, valvular disease, and cardiomyopathy. The presence of strokes in different cerebral circulations or evidence of systemic embolization strongly suggests embolic stroke. Although some studies have suggested that embolic strokes are "lightninglike" in onset, not preceded by TIAs, and more often associated with seizures at onset, these features are not always reliable. Although most embolic strokes occur in middle or old age, the sudden onset of an ischemic stroke in a person under age 35 with no atherosclerotic risk factors suggests an embolic event.

Lacunar events almost always occur in patients with hypertension. Maximum deficit may be present immediately or may occur in a "stuttering" or slowly progressive fashion. The clinical differentiation of atypical lacunar syndrome from atherosclerotic syndromes is often difficult, but classic lacunar syndromes, especially pure motor hemiparesis, should be recognized so that unwarranted invasive diagnostic procedures may be avoided. Treatment of lacunar strokes consists of treatment of underlying hypertension. Since lacunar strokes involve deep structures (basal ganglia, internal capsule, brainstem), patients with lacunar stroke do not have aphasia, sensory neglect, visual field loss, or other deficits caused by cortical dysfunction. Small lacunar infarctions of deep structures may be seen on CT scan or MRI, and may be multiple. Depending on their location, some lacunar infarctions are asymptomatic.

Rare causes of stroke should be considered, especially in younger individuals, by seeking evidence of collagen diseases, hematologic diseases (sickle cell disease and coagulopathies), or history of recent long-bone fracture (fat emboli syndrome).

The main goal of treatment is to prevent further events by treating the underlying cause. Atherosclerotic risk factors, especially hypertension, should be reduced or eliminated. Other treatment of stroke and TIA due to atherosclerotic disease remains controversial. There is more evidence for a beneficial effect of aspirin than any other agent. New antiplatelet drugs are being developed which may be more effective. Anticoagulation with coumadin is of no conclusive value in atherosclerotic TIA and stroke, although it is the treatment of choice for embolic strokes and TIAs. The role of carotid endarterectomy in the management of carotid distribution TIAs has long been debated. If the patient has an ulcerated plaque or internal carotid stenosis of greater than 75% in the vascular distribution of symptoms, many clinicians would suggest surgery. Other factors should be considered, including the patient's age, presence of concurrent medical illness, and risk of operative morbidity and mortality at one's institution. The many other proposed or investigational medical and surgical therapies for ischemic TIA and stroke await further documentation of efficacy.

In addition to risk for further stroke, a history of ischemic cerebrovascular events clearly increases a patient's risk for coronary disease, which becomes four times that of other persons the same age. The 5-year mortality following stroke is about 50%, with death largely from cardiac causes. These statistics must be borne in mind when considering the efficacy of any therapy for ischemic stroke. Also, individual patients should be questioned carefully for any history or symptoms of coronary artery disease.

Differentiating between ischemic stroke and intracranial hemorrhage is usually easy because the latter is often much more catastrophic with precipitous onset of severe headache, nausea and vomiting, and clouding of consciousness. Hemorrhages of all etiologies tend to occur in younger patients than those afflicted by ischemic stroke. Although it is often said that ischemic strokes occur at rest or during sleep, whereas hemorrhages occur during straining or exertion, this is not always a reliable rule. Although headaches are more common in hemorrhage, they can also occur in ischemic stroke, and not every patient with a hemorrhage has a headache. Vomiting within 15 minutes of onset is highly suggestive of hemorrhage. Small intracerebral hematomas may be indistinguishable from ischemic stroke. The differentiation is readily made by CT scan, which has become almost routine in evaluation of patients with stroke and is mandatory if anticoagulation is contemplated.

Intracerebral hematomas due to hypertension have a predilection for the putamen, thalamus, pons, and cerebellum, but can occur in the cerebral white matter. Typically, the patient is a middle-aged or elderly hypertensive with a sudden headache and focal deficit with diagnosis confirmed by CT scan. *Cerebellar hematomas* are true emergencies and cause nausea, ataxia, nystagmus, gaze palsies, and decreased consciousness. A striking feature is inability to walk or stand. Immediate surgical evacuation is usually required to prevent brainstem compression, cerebellar tonsillar herniation, or obstructive hydrocephalus.

Subarachnoid hemorrhage due to *ruptured saccular aneurysm* must always be suspected in a person with the sudden onset of a severe occipital headache, especially if there is associated confusion, altered responsiveness, or stiff neck. If the patient can provide a history, he often dramatically describes the pain as "the worst headache of my life." Headache may spread to the neck, intrascapular area, or even the low back. Many patients exhibit irritability, restlessness, and disturbed autonomic functions. Although there are usually no focal symptoms or signs, some aneurysms, for example those of the middle cerebral artery, may rupture into the brain parenchyma and be confused with hematomas due to hypertension or arteriovenous malformations. In such circumstances, selective cerebral arteriography will identify the cause. If the clinical situation suggests subarachnoid hemorrhage, a CT scan of the head is indicated. Although blood is seen in the subarachnoid spaces or basal cisterns in most patients, small hemorrhages or older hemorrhages where blood has been absorbed may be missed by CT scan, requiring lumbar puncture. If a subarachnoid hemorrhage is present, complete selective cerebral arteriography to demonstrate a saccular aneurysm is mandatory, since surgical clipping should be undertaken to prevent rebleeding. The management of aneurysms is complex and may also require treatment for vasospasm (which results in delayed superimposed ischemia) or communicating hydrocephalus.

With long-term neurologic deficits due to cerebrovascular disease, it is important to assess the patient's ability for functional living. The quality of life of many patients is improved considerably by participation in a comprehensive rehabilitation program.

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